Health Care Provider Fact Sheet

Disease Name — Glutaric acidemia, type 1

Alternate name(s)	Glutaric aciduria I, Glutaryl-CoA dehydrogenase deficiency
Acronym	GA1, GAI
Disease Classification	Organic Acid Disorder
Variants	Yes
Variant name	Riboflavin responsive GA1
Symptom onset	Infancy (typically 2- 37 months)
Symptoms	Macrocephaly may be present at birth, acute encephalitic-like crises; neurodegenerative disorder with spasticity, dystonia, choreoathetosis, ataxia and dyskinesia, seizures, hypotonia, death due to Reye-like syndrome.
Natural history without treatment	Possible developmental delay due to encephalitis-like crisis; neurologic deterioration including spasticity, dystonic cerebral palsy. May have neurologic signs with normal IQ. Some individuals may be asymptomatic.
Natural history with treatment	If instituted before any damage occurs, normal outcome may occur. Risk for neurologic damage is highest in first few years. Some evidence that treatment may slow neurologic deterioration.
Treatment	Lysine and tryptophan restricted diet, riboflavin supplementation, carnitine supplementation. Rapid treatment of intercurrent illness with intravenous glucose, carnitine and appropriate supportive measures.
Other	Profuse sweating has been reported. Neuroradiographic findings of frontotemporal atrophy on CT or MRI with increased CSF containing spaces in the sylvian fissures and anterior to the temporal lobes. Also decreased attenuation in cerebral white matter on CT and increased signal intensity on MRI. Basal ganglia changes.
Physical phenotype	Macrocephaly, cerebral palsy
Inheritance	Autosomal recessive
General population incidence	1:40,000 in Caucasians and 1:30,000 in Sweden
Ethnic differences	Yes
Population	Old Amish and Ojibway Indians in Canada
Ethnic incidence	1/10 carrier frequency
Enzyme location	Mitochondria; liver, kidney, fibroblasts and leukocytes
Enzyme Function	Metabolizes lysine, hydroxylysine and tryptophan
Missing Enzyme	Glutaryl-CoA dehydrogenase
Metabolite changes	Increased glutaric acid in urine, increased glutaric acid and 3-hydroxyglutaric acid in plasma, 3-hydroxyglutaric and glutaconic acid in urine.
Gene	GCDH
Gene location	19p13.2
DNA testing available	Yes.
DNA testing detail	No common mutations outside of Old Amish (A421V)
Prenatal testing	Enzymen activity in CVS and amniocytes
MS/MS Profile	Elevated C5DC - can be missed some patients
OMIM Link	www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=231670
Genetests Link	www.genetests.org
Support Group	Organic Acidemia Association www.oaanews.org Save Babies through Screening Foundation www.savebabies.org Genetic Alliance www.geneticalliance.org